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10/518,956

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EXAMINER

DANG, IAN D

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

11/25/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                   |  |
|------------------------------|--------------------------------------|-----------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/518,956 | <b>Applicant(s)</b><br>HAJ ET AL. |  |
|                              | <b>Examiner</b><br>IAN DANG          | <b>Art Unit</b><br>1647           |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 October 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 175-196 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 175-196 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 December 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
- ☒ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                        |                                                                   |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/14/2008, 11/04/2008</u> .                                  | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/14/2008 has been entered.

#### ***Status of Application, Amendments and/or Claims***

The amendment of 14 October 2008 has been entered in full. Claims 1-174 have been cancelled and claims 175-196 have been newly added.

Claims 175-196 are under examination.

#### ***Specification***

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

#### ***Claim Rejections - 35 USC § 112, Second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 175-196 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 175-196 are indefinite because they use acronym TREK without first defining what they represent in the independent claims (see for example, "TREK", etc.). While the

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claims can reference acronyms, the material presented by the acronym must be clearly set forth at the first use of the acronym. The recitation of TWIK-related potassium channel (TREK) in claim 175 would overcome the rejection.

Claims 175-196 are indefinite because the method of the instant application is missing essential method steps or conclusion in claims 175 and 186. It is not clear how the application of a magnetic field is all that is required to produce cartilage. The recitation of, for example, "applying a magnetic field .... thereby generating cartilage", or some step which would tie into the preamble, would obviate the rejection.

Appropriate correction is required.

### **Rejection Withdrawn**

#### ***35 USC § 112, First paragraph (Written Description)***

Applicant's response and arguments filed on 10/14/2008 have overcome the rejection regarding magnetizable particles, the composition of the magnetizable particles, and magnetizable particle associated with an antibody as applied to claims 175-196 under 35 USC 112, First paragraph (Written Description). At pages 7-10 of the response, Applicants have provided the US Patent 6,548,264 to overcome the rejection regarding magnetizable particles and the composition of the magnetizable particles as recited in claims 182-184 and 193-195. In addition, Applicants have added the limitation "magnetizable particles tagged with one or more antibodies specific for TREK potassium ion channels" as recited in claims 175 and 186 to overcome the rejection regarding magnetizable particle associated with an antibody. The rejection regarding magnetizable particle associated with an antibody, magnetizable particles, and the composition of the magnetizable particles as applied to claims 175-196 under 35 USC

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112, First paragraph (Written Description) has been withdrawn.

### **Rejection Maintained**

#### ***Claim Rejections - 35 USC § 112. First paragraph (Enablement)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The newly added claims 175-196 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) up-regulation of osteopontin in response to a magnetic field in the presence of anti-TREK antibody bound to magnetic nanoparticles binding to TREK channel in mesenchymal cells, and (2) the production of cartilage matrix proteins in mice by implanted human mesenchymal stem cells in the presence of magnetic nanoparticles bound to cells via an anti-TREK antibody in response to time varying magnetic fields, does not reasonably provide enablement for (A) an *in vitro* method for the generation of cartilage tissue from mammalian cartilage cells expressing mechanosensitive TREK potassium ion channels, and (B) a method of the generation of new cartilage tissue in a patient, wherein the new cartilage tissue is generated from cartilage cells expressing the mechanosensitive TREK potassium ion channels. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Although Applicants have overcome numerous issues rejected under 35 USC 112, First paragraph (Enablement) by adding the new claims 175-196, these newly added claims are also

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rejected under 35 USC 112, First paragraph (Enablement). Upon further review of the declaration filed 01/08/2008, the Examiner has determined that Applicants have not satisfied the enablement requirements for the generation of cartilage tissue using magnetizable particles bound to an anti-TREK antibody. Applicants are enabled for (1) up-regulation of osteopontin in response to a magnetic field in the presence of anti-TREK antibody bound to magnetic nanoparticles binding to TREK channel in mesenchymal cells, and (2) the production of cartilage matrix proteins in mice by implanted human mesenchymal stem cells in the presence of magnetic nanoparticles bound to cells via an anti-TREK antibody in response to time varying magnetic fields.

At page 10 of the response, Applicants indicate that the amendments made to the claims correlate with the subject matter which the Examiner has indicated is enabled, i.e. the generation of cartilage tissue using magnetizable particles bound to an anti-TREK antibody. In view of the amendments, Applicants allege that the claimed subject matter now directly correlates with results showing the successful generation of cartilage tissue using magnetizable particles tagged with anti-TREK antibody.

Applicants' arguments and response have been fully considered but are not found persuasive. Upon further consideration, the Examiner has determined that Applicants have not satisfied the enablement requirements for the generation of cartilage tissue using magnetizable particles bound to an anti-TREK antibody. After a careful review of the Exhibit B disclosed in the declaration filed 01/08/2008, the Examiner has determined that Exhibit B provides evidence for the production of cartilage matrix proteins in mice by implanted human mesenchymal stem cells in the presence of magnetic nanoparticles bound to cells via an anti-TREK antibody.

However, there is insufficient evidence for a method for the generation of cartilage tissue using magnetizable particles bound to an anti-TREK antibody, since the synthesis of cartilage

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matrix proteins is distinct from the production cartilage tissue. Cartilage tissue is a type of dense connective tissue composed of the specialized cells called chondrocytes, a ground substance rich in proteoglycan, and elastin fibers and Applicants have only provided evidence for the presence of cartilage matrix protein expressed by chondrocytes. Exhibit B does not provide any evidence for the presence of the other 2 components of the cartilage tissue that include the ground substance rich in proteoglycan and elastin fibers. In addition, the human mesenchymal stem cells disclosed in Exhibit B are not equivalent to cartilage cells as recited in claims 175 and 186, since these cells have different functions and biological activities. It follows that the generation of protein matrix from mesenchymal stem cells in Exhibit B cannot be used to extrapolate to generation of protein matrix of cartilage cells.

Thus it would require undue experimentation to practice the invention commensurate in scope with the claims because the claims are broadly drawn to a method for the generation of cartilage tissue with cartilage cells while the evidence supports a method for upregulating proteins part of the cartilage protein matrix with mesenchymal stem cells.

Moreover, although Applicants disclose examples (1) up-regulation of osteopontin in response to a magnetic field in the presence of anti-TREK antibody bound to magnetic nanoparticles binding to TREK channel in mesenchymal cells (Exhibit A, filed 01/08/2008), and (2) the production of cartilage matrix proteins in mice by implanted human mesenchymal stem cells in the presence of magnetic nanoparticles bound to cells via an anti-TREK antibody in response to time varying magnetic fields (Exhibit B, filed 01/08/2008), the specification does not provide any guidance regarding the nexus between the up-regulation of osteopontin or the production of cartilage matrix proteins in mice and the generation of cartilage tissue *in vitro* or in a patient.

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Finally, the specification does not provide any guidance regarding how these examples would be indicative of an *in vitro* method for the generation of cartilage tissue or the method for the generation of new cartilage tissue in a patient from cartilage cells expressing mechanosensitive TREK potassium ions channels. Since the Examiner has concerns about Applicants' examples being art accepted, the Examiner requests that Applicants support the assertion that their models were well known in the art to be indicative of the *in vitro* method for the generation of cartilage tissue or the method for the generation of new cartilage tissue in a patient from cartilage cells expressing mechanosensitive TREK potassium ions channels. Without providing such disclosures, the claimed methods reciting in the claims of the instant application would require undue experimentation.

Thus one of skill the art would not be able to use the claimed (A) an *in vitro* method for the generation of cartilage tissue from mammalian cartilage cells expressing mechanosensitive TREK potassium ion channels, and (B) a method of the generation of new cartilage tissue in a patient, wherein the new cartilage tissue is generated from cartilage cells expressing the mechanosensitive TREK potassium ion channels because the specification has not provided enough information.

### **Conclusion**

No claim is allowed.

### **Information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IAN DANG whose telephone number is (571)272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.



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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang  
Patent Examiner  
Art Unit 1647  
November 18, 2008

/Robert Landsman/  
Primary Examiner, Art Unit 1647